Practitioner's Docket No.: 789_070 CON2 ***PATENT***

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of: Toshikazu HIROTA and Takao OHNISHI

Serial No.: 10/757,264 Group Art Unit: 1634

Filed: January 14, 2004 Examiner: Betty J. Forman

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For: BIOCHIP

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Tara L. Preston

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REQUEST FOR RECONSIDERATION

Sir:

In response to the PTO paper mailed November 20, 2006, and the Office Action mailed May 12, 2006, Applicants respectfully request reconsideration and withdrawal of the rejections of record based on the following arguments.

Examiner Forman is thanked for courtesies extended to Applicants' representatives during a telephonic interview on August 22, 2006. During the interview, Examiner Forman stated that the Rule 132 Declaration entered in the parent case should be put on record in the present application to overcome the non-ink jet references. Accordingly, attached hereto is the Rule 132 Declaration of Mr. Toshikazu Hirota that was filed in the parent case. Mr. Hirota attests to the quantitative results of experimentation which proves that the claimed ink-jet process provides a structurally distinct biochip from biochips fabricated using conventional

pin-head techniques. Entry and consideration of the Rule 132 Declaration are respectfully requested.

1. Claims 3, 4, 7, 8, 11, 12 and 13 were rejected under §102(e) over Audeh et al., or Mirzabekov et al., or Chenchik et al. in paragraphs 3, 4 and 5, respectively, of the Office Action. These rejections are respectfully traversed.

Pending independent claims 1, 3 and 13 each recite, among other things, that a plurality of spots of capture material are supplied onto a base plate by means of an ink-jet system. Claim 1 recites that the capture material spots have different sizes, and claims 3 and 13 each recite that the concentration of the capture material in the capture solutions varies from spot to spot. Each of the pending independent claims further recite that all of the capture solution spots have uniform detection sensitivity.

The ink-jet process of supplying capture solutions onto the base plate is quantitatively proven (by the inventor's experimentation discussed below) to produce biochips that include capture material spots having uniform detection sensitivity. This result is possible because the ink-jet delivered capture material spot sizes and capture material concentration per sample spot are accurately and precisely controlled in every instance. Such accurate, precise and reproducible capture material spot sizes and capture material concentration per sample spot, which, again, are quantitatively proven to be attributable to the ink-jet process, are not attainable using conventional pin-head array techniques (discussed below).

The PTO admits that Audeh and Chenchik do not disclose the use of an ink-jet system to supply probe samples onto substrates (see Office Action page 3, lines 7-8 and page 7, lines 3-4).

The PTO is arguing that the Peltier thermostated pin disclosed in Mirzabekov is an ink-jet device. Applicants respectfully submit that the Mirzabekov patent explicitly shows that a Peltier thermostated pin is a pin-spotting device, wherein a portion of the device physically contacts the base plate surface and includes a Peltier element to control the temperature of the pin (see Mirzabekov patent column 11, lines 45-48;

column 12, lines 8-20, especially lines 18-20). Examiner Forman is respectfully requested to note that based on these citations to Mirzabekov alone, the statement on page 8 of the Office Action that Mirzabekov's disclosure of a Peltier thermostated pin is equivalent to an ink-jet system is incorrect.

In view of the foregoing, it is clear that none of the applied references discloses the use of an ink jet system to form a biochip, as claimed. To date, however, Examiner Forman has not given the "ink jet" feature recited in the pending claims any patentable weight.

Federal Circuit case law and the MPEP clearly state that, when dealing with product-by-process claim limitations, determination of patentability is based on the product itself (see MPEP §2173.05(p) discussing the case law in existence regarding product-by-process claims). These authorities make clear that, if the process by which the product is formed yields a structurally distinct product, then the product-by-process claim limitation must be given weight in defining patentable subject matter over the prior art product. Based on the results of the quantitative experimentation (i.e., shown in the table and graph discussed below), it is undeniable that the claimed ink-jet process provides a structurally distinct biochip product over biochips formed using the pin-head contact devices disclosed in the applied prior art of record (i.e., Audeh, Mirzabekov and Chenchik).

The ink-jet process, as compared to conventional pin-head contact methods, provides a structurally distinct biochip, because of the non-contact nature of the ink-jet process. In accordance with the invention, a first ink-jet sample spot that has a desired spot size (e.g., pending claim 1) and/or a desired capture material concentration (e.g., pending claims 3 and 13) is supplied onto a base plate and allowed to dry. A second ink-jet sample spot, which, for example, can have the same or a different spot size in relation to the first ink-jet sample spot and/or the same or a different capture material concentration, is then supplied on top of the dried first ink-jet sample spot. Due to the non-contact nature of the ink-jet process, the integrity of the dried first ink-jet sample

spot is not affected by the delivery of the second ink-jet sample spot. This is not the case with conventional pin-head methods, as discussed below.

Conventional pin-head spotting devices, such as those disclosed in Audeh, Mirzabekov and Chenchik, use pin heads that are brought into contact with the support surface when delivering probe sample solutions onto the support. The pin heads are dipped into sample wells containing the probe sample solution to collect individual probe samples and spot the probe samples onto the substrate by physically tapping the end of each of the pin heads against the upper surface of the substrate. After each probe sample is spotted onto the substrate, each of the pin heads is washed with water and ethanol and air dried before the pin heads are re-inserted into the sample wells to collect another batch of probe sample solution to be subsequently supplied onto the substrate. After the previously supplied probe sample solution spots have dried, another series of probe sample solution spots are subsequently placed onto the substrate using the washed pin heads in the arraying device. During the application of all subsequent probe sample spots, the pin heads contact the previously applied dried sample solution spots to deposit the subsequently supplied probe sample spots on top of the previously supplied spots.

When the pin head tips contact the dried sample spots, some portion of the spot sticks to the pins, and thus a portion of the previously supplied dried spots is removed during the delivery of every subsequent supplied probe sample spot. As will be shown from the quantitative results of the experimentation discussed below, because the pin heads contact all of the previously supplied probe samples and come into physical contact with the substrate every time a subsequent probe sample spot is deposited in the array, the fine degree of accuracy and precision in spot size formation and capture material concentration per sample spot attributable to the claimed ink-jet process is not possible when the sample spots are pin-spotted onto the support surface.

The table attached to Mr. Hirota's Declaration shows the results of a direct comparison between the variations of fluorescent signal intensities emitted from

ink-jet delivered capture solution spots having target capture material concentrations of "1", "2" or "3", and capture material spots having the same relative capture material concentrations delivered by a pin-head method. A total of 60 spots were formed on a base plate. Each spot within a first group of 30 spots was formed using the ink-jet method, while each spot in the second group of 30 spots was formed using the pin-head method. After the first drops were allowed to dry, a second sample drop was supplied using the ink-jet method to 20 of the 30 spots in the first group, and a second sample drop was supplied using the pin-head method to 20 of the 30 spots in the second group. After the second drops were allowed to dry, a third sample drop was supplied using the ink-jet method to 10 of the two-drop spots in the first group, and a third drop was supplied using the pin-head method to 10 of the two-drop spots in the second group. The finished test slide, therefore, had two groups of 30 spots, and within each group there were 10 one-drop spots, 10 two-drop spots, and 10 three-drop spots.

A solution including a target material capable of reacting with the corresponding capture materials in the capture material spots formed on the base plate was then supplied onto each spot. Again, the capture solutions used to form the spots contained relative concentrations of capture materials (i.e., target concentration of capture material 1, 2 or 3) that were adapted to specifically react with the target materials in the target material solution which was, for example, a positive control. The reaction between the capture material spots and the target material solution caused a fluorescent signal to be emitted from each reacted capture solution spot. The fluorescent signal intensity value from each spot was obtained by subtracting background fluorescence, such as, for example, fluorescence emitted from the base plate itself, from the total fluorescence emanating from the reacted capture material spots and the base plate. The capture material fluorescent signal intensities were detected and measured using a conventional scanning apparatus.

The table attached to Mr. Hirota's Declaration shows that the fluorescent signal intensities emitted from each of the individual spots within each capture spot group of pin-head delivered capture solution spots vary significantly from one another in comparison to the much smaller variation between the signal intensities emitted from the individual spots within each capture spot group of ink-jet supplied capture material spots. For example, while the standard deviation of signal intensities between ink-jet delivered spots in the relative target concentration capture spot groups 1-3 was 310, 311 and 435, respectively, the standard deviation of signal intensities between pin-head delivered spots in the same relative target concentration capture spot groups 1-3 was 656, 889 and 979, respectively. The lower standard deviation between the ink-jet delivered capture material spots, as compared to the higher standard deviation between the pin-head delivered capture material spots, proves that the claimed ink-jet process consistently delivers capture material spots having a more precise, desired amount of capture material per sample spot. This is due to the non-contact nature of the ink-jet method.

The relatively higher standard deviation between the pin-head delivered sample spots is due to the disruptive nature of the contact (between the pin and the base plate) that is necessary to perform the pin-head method. These results show that the degree of accuracy and precision in capture material per spot attributable to the claimed ink-jet process is not attainable using prior art pin-head arraying devices, such as those disclosed in Audeh, Mitzabekov and Chenchik.

The comparative table of signals also shows that a significant variation exists between the standard deviation of fluorescent signal intensities emitted from each group of capture material spots delivered using a pin-head device when compared to the signal intensities of those same groups of capture material spots supplied onto the base plate via the ink-jet process. For example, while the standard deviation values for the signal intensities between the ink-jet delivered spots in relative target concentration capture spot groups 1 and 2 are practically identical (i.e, the standard

deviations are 310 and 311, respectively), a much wider gap exists between the standard deviation values for the signal intensities between the pin-head delivered spots in relative target concentration capture spot groups 1 and 2 (i.e, the standard deviations are 656 and 889, respectively).

The practically identical standard deviation values for the signal intensities emitted from the ink-jet delivered capture material spots in relative target concentration capture spot groups 1 and 2 is attributable to the non-contact nature of the ink-jet process. That is, the dried first ink-jet sample spot (having a target concentration of 1) is not affected by the delivery of the second ink-jet supplied sample spot (to provide an overall target concentration of 2). The standard deviation values for the signal intensities between the pin-head delivered spots in relative target concentration capture spot groups 1 and 2 varies widely due to the contact nature of the pin-head method. These results show that the more precise, desired amount of capture material per sample spot attributable to the claimed ink-jet process is not attainable using prior art pin-head arraying devices, such as those disclosed in Audeh, Mitzabekov and Chenchik.

The graph attached to Mr. Hirota's Declaration also provides quantitative proof that the non-contact nature of the claimed ink-jet process makes it possible to reproducibly deliver a more precise, desired amount of capture material per sample spot as compared to prior art pin-contact methods. The graph shows the existence of a linear relationship between the emitted signal intensities (which correspond to the relative target concentrations of each of the sample spots) of each of the ink-jet capture spot groups 1-3. That is, there is a clear linear relationship between the 3 groups. While the signal intensity values for ink-jet capture spot groups 1-3 are tightly packed around their respective average signal intensity values, it is difficult to ascertain whether the emitted signal intensity values for each of the pin-head capture spot groups 1-3 even belong to the same capture spot group. For example, it is clear that the signal intensities for the pin-head capture spot groups 1-3 are widely scattered

and there are several instances in which the signal intensity values for one capture spot group overlap with the signal intensity values of another capture spot group. Accordingly, the graph results provide further proof that the more exact, desired and reproducible amount of capture material per sample spot attributable to the claimed ink-jet process is not attainable using prior art pin-contact arraying devices.

The above experiments quantitatively prove that use of an ink-jet process, as claimed, precisely delivers capture material spots having a more accurate and reproducible capture material concentration and spot size in comparison to capture material spots that are supplied onto a base plate using conventional pin-head techniques. Consequently, the results of this experimentation clearly show that the claimed ink-jet process provides a structurally distinct biochip in comparison to a biochip that is fabricated using conventional pin-head methods.

In view of all of the foregoing, reconsideration and withdrawal of the §102(e) rejections over Audeh, Mirzabekov and Chenchik are respectfully requested.

2. Claims 1, 2, 5, 6, 9 and 10 were rejected under §103(a) over Audeh in view of Dean, or Mirzabekov in view of Dean, or Chenchik in view of Dean in paragraphs 7, 8 and 9, respectively, of the Office Action.

The above discussion and quantitative experimental results shown in the attached table and graph clearly show that the claimed invention provides a structurally distinct biochip in comparison to the biochips produced using conventional pin-head type arraying devices similar to those disclosed in each of Audeh, Mirzabekov and Chenchik. The PTO's reliance upon Dean for disclosure that a linear relationship exists between spot concentration and spot size does not change the fact that the claimed biochip is patentably distinct over the biochips disclosed in the primary references for the reasons explained above. Consequently, the §103(a) rejections are erroneous and should be withdrawn for this reason alone.

Moreover, there is no disclosure in any of the applied prior art references that would have motivated one skilled in the art to abandon the conventional pin-head

contact devices disclosed in Audeh, Mirzabekov and Chenchik in favor of an ink-jet system (as claimed) for any reason, let alone the above-discussed benefits quantitatively proven to be attributable to the ink-jet process as first discovered by Applicants herein.

In view of all of the foregoing, reconsideration and withdrawal of the §103(a) rejections are respectfully requested.

3. Claims 1-13 were rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-13 of U.S. Patent No. 6,753,144. Applicants respectfully request that this rejection be held in abeyance until all of the prior art rejections are withdrawn.

If the Examiner believes that contact with Applicants' attorney would be advantageous toward the disposition of this case, the Examiner is herein requested to call Applicants' attorney at the phone number noted below.

The Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. 50-1446.

Respectfully submitted,

November 29, 2006
Date

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SPB/TE/tlp

Enclosures: Rule 132 Declaration of Toshikazu Hirota
Comparative Table of Signals
Comparative Graph of Signal Intensities

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